WO 2005/049793 PCT/US2004/035643

What is claimed is:

- 1. A nucleic acid comprising
- a) a first nucleotide sequence encoding a pro-apoptotic protein selected from the group consisting of DR4, tBid or a biologically active fragment thereof and any combination thereof, and
- b) a second nucleotide sequence encoding a tumor-specific promoter selected from the group consisting of survivin promoter, MUC-1 promoter, htert promoter, CEA promoter, PSA promoter, alpha-fetoprotein promoter or a biologically active fragment thereof and any combination thereof, wherein second nucleotide sequence is operably linked to and directs the expression of the first nucleotide sequence.
- 2. The nucleic acid of claim 1, further comprising a third nucleotide sequence encoding a pro-apoptotic mediator selected from the group consisting of Bax, Smac, caspase 3, TRAIL or a biologically active fragment thereof and any combination thereof.
 - 3. A vector comprising the nucleic acid of claims 1 or 2.
- 4. The vector of claim 3, wherein the vector is selected from the group consisting of AAV vector, lentivirus vector, adenovirus vector and a nonviral vector.
- 5. A composition comprising the nucleic acid of claims 1 or 2 or the vector of claims 3 or 4 in a pharmaceutically acceptable carrier.
 - 6. The composition of claim 5, further comprising a chemotherapeutic agent.
- 7. A method of treating a cancer in a subject, comprising administering to the subject an effective amount of the nucleic acid of claims 1 or 2, the vectors of claims 3 or 4 or the composition of claims 5 or 6 to the subject, thereby treating the cancer in the subject.
- 8. A method of producing a viral vector comprising the nucleic acid of claim 1, comprising introducing into a cell in which viral vectors are produced:

WO 2005/049793 PCT/US2004/035643

a) a nucleic acid comprising a nucleotide sequence encoding one or more proapoptotic proteins, operably linked to one or more tumor-specific promoters and a viral packaging signal;

- b) an siRNA construct and/or an antisense sequence that targets the nucleotide sequence encoding the one or more pro-apoptotic proteins of (a), either prior to, or simultaneously with introducing the nucleic acid of (a) into the cell; and
- c) nucleic acid encoding viral structural proteins and/or nonstructural proteins necessary to produce viral structural proteins that package nucleic acid into a viral vector particle, under conditions whereby the nucleic acid of (a) is packaged into a viral vector particle, thereby producing the viral vector comprising the nucleic acid of claim 1.
- 9. A method of producing a viral vector comprising the nucleic acid of claim 1, comprising introducing into a cell in which viral vectors are produced:
- a) a nucleic acid comprising a nucleotide sequence encoding one or more proapoptotic proteins, operably linked to one or more tumor-specific promoters and a viral packaging signal;
- b) a nucleic acid encoding bcl-2 under the direction of an active promoter, either prior to, or simultaneously with introducing the nucleic acid of (a) into the cell; and
- c) nucleic acid encoding viral structural proteins and/or nonstructural proteins necessary to produce viral structural proteins that package nucleic acid into a viral vector particle, under conditions whereby the nucleic acid of (a) is packaged into a viral vector particle, thereby producing the viral vector comprising the nucleic acid of claim 1.